

The biomedical sciences and the need for less-inhumane animal procedures

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Summary

The use of humane endpoints is considered in relation to Russell and Burch's concept of direct and contingent inhumanity in the context of laboratory animal experimentation, and the application of the Three Rs (replacement, reduction and refinement) as a means of diminishing or removing such inhumanity. It is argued that scientific justification of the purpose of a procedure in meeting the essential needs of man and other animals is an inescapable requirement, upon the strength of which the humanity or inhumanity of the overall use of a procedure ultimately depends, irrespective of the degree of refinement achieved through good experimental design or of the humaneness of the endpoint used in the procedure. It is concluded that the conference was really about less-inhumane endpoints, and that wider recognition of this truth would be the stimulus to further effort and further progress.

I am very glad that this conference on humane endpoints has taken place, and that it has followed so closely after the important meeting of OECD nominated national experts, held in Zeist a week earlier to discuss a draft OECD guidance document on humane endpoints. Wondering what I could usefully contribute, as one primarily involved with the development and validation of replacement alternatives, rather than the reduction or refinement of alternatives, I turned to *The Principles of Humane Experimental Technique* (Russell & Burch 1959) for inspiration. Somewhat surprisingly, and undoubtedly courageously, Russell and Burch decided to discuss humane experimental technique in terms of the *concept of inhumanity*. They said that 'the central problem is that of determining what is and is not humane, and how humanity can be promoted without prejudice to scientific and medical aims'. Emphasizing that their analysis implied no ethical criticism of persons practising any particular laboratory animal proce-

dures, they recognized two kinds of inhumanity:

- *Direct inhumanity*—the infliction of distress as an unavoidable consequence of the procedure applied; and
- *Contingent inhumanity*—the infliction of distress as an incidental and inadvertent by-product of the use of a procedure.

They then went on to develop what we now know as the *Three Rs concept*, as a means of diminishing or removing direct and/or contingent inhumanity. Their proposal of the Three Rs concept led, in turn, to the *concept of alternatives*, defined to include 'all procedures which can completely replace the need for animal experiments, reduce the number of animals required, or diminish the amount of pain or distress suffered by animals in meeting the essential needs of man and other animals'. This special use of the word *alternatives* is central to the theme of the argument I wish to develop here, but first I want to consider the use of some other terms.

*This article represents the personal views of the author.

In my dictionary (The Reader's Digest 1979), *humane* means 'benevolent' and 'compassionate' and, as if this conference had been foreseen by its compilers, 'tending to refinement', whereas the meaning of *inhumane* can range from 'brutal' and 'barbarous' to 'unfeeling' and 'unsympathetic', and *cruelty* can mean 'liking to inflict pain' or 'indifferent to the pain of others'. I have come across very few incidences of outright brutality or barbarity, or of flagrant cruelty, on the part of those who use laboratory animals, although sadly there have been some. However, examples of lack of awareness of animal suffering, of indifference, and of lack of feeling and sympathy, are encountered much more frequently.

Charles Hume, founder of the Universities Federation for Animal Welfare and, by the way, the principal instigator of Russell and Burch's project, put it another way in *Blind Spots*, a disturbing chapter in his marvellous book, *Man and Beast* (1959). Referring to those involved in the past in upholding slavery and the exploitation of children (e.g. the use of 'climbing boys' as chimney sweeps), he said: 'These apparently callous ancestors of ours were decent, humane, cultured people like ourselves. They simply had a blind spot toward cruelties that were sanctioned by custom'. No scientists involved in the use of laboratory animals can fall back on this kind of excuse, although I have been staggered by recent evidence of ignorance of the legal frameworks within which animal research scientists have to work, based on national and EU legislation.

The theme on which I want to focus is the importance of that part of the definition of alternatives which emphasizes the importance of *meeting the essential needs of man and other animals*, when procedures are applied to laboratory animals which may cause them pain, distress, suffering or lasting harm. In other words, necessity must be satisfactorily established. Otherwise, however humane the endpoints applied may be, the overall use of the animals concerned will inescapably involve inhumanity. The commonly-used argument that the use of animals in biomedical research is justifiable because it is necessary, is discussed at length in *Lives*

in the Balance—The Ethics of Using Animals in Biomedical Research (Smith & Boyd 1991). It is clear that the concept of necessity is weak, both in a moral sense and in a legal sense, as the validity of any claim of necessity is utterly dependent on the legitimacy and value of the purpose which is to be served by the studies.

How a purpose is achieved is important, and that is why the refinement of procedures, including the optimization of experimental design and the use of more-humane endpoints, is important. Nevertheless, at the risk of repeating myself, I must emphasize that a procedure cannot be considered humane in the absence of a strong case for it to be regarded as scientifically justifiable on the basis of it being necessary, or even essential, because of its purpose. This is particularly important when we consider the direct inhumanity which is inevitably involved in many toxicity test procedures, and in the efficacy and safety testing of biological products such as vaccines. Those conducting such tests often claim that what they are doing is necessary, merely because it is required by regulations laid down by one or more of the authorities responsible for the manufacture, marketing and use of chemicals and products of various kinds. In my opinion, such claims of exemption from moral responsibility are facile and unacceptable. They are reminiscent of the sad feelings of the kind slave owners portrayed in Harriet Beecher Stowe's *Uncle Tom's Cabin* (1852), who knew that what they were doing was wrong, but who took shelter in the belief that the system they were caught up in was bigger than them, and beyond their capacity to change or influence greatly. It was sanctioned by the custom of the times. In reality, they were no less culpable than the overtly cruel slave owners characterized so frighteningly in this dramatic novel. Thus, there is no escape from the Fourth R, which, though unwritten, underlies the whole of *The Principles of Human Experimental Technique*, namely, the burden of Responsibility, placed on all those who are involved, directly or indirectly, in any way.

In one of the last chapters in their book, Russell and Burch discussed *The Factors*

Governing Progress, which they subdivided into two classes: personality factors and sociological factors. They went so far as to focus on two *pathological* personality variables, the authoritarian factor and the revolutionary factor. There are still some scientists who claim the right to do whatever research on animals they wish to do, without the fetters of legal regulations and controls, and there are some revolutionaries who resort to extreme measures in pursuance of their anti-vivisectionist cause. I am a revolutionary at heart, but my head makes me resolved to work with rational people as the best means of achieving the goals I seek. All those who have contributed in any way to this conference are occupiers together of that extensive, rational, middle ground between the authoritarian and revolutionary extremes.

In discussing the sociological factors, Russell and Burch considered the significance of conflicts between humanity and efficiency, flexibility and rigidity, and knowledge and ignorance, as well as the importance of legal frameworks and controls, of education and training, and of communication and debate. All of these factors are reflected in the discussions at this conference, to the great credit of all concerned.

I would like to summarize, as I was asked to do at another recent conference, my fears and hopes for the future. I am worried that the small steps we are taking in achieving reduction, refinement and replacement, will be overwhelmed by other politically-motivated activities which are having counter-effects. As examples, I can cite a plan by the US Environmental Protection Agency, the Chemical Manufacturers Association and the Environmental Defense Fund to have nearly 3000 high production volume chemicals tested in a series of animal procedures, in order to provide 'missing toxicity data'. This is the ultimate example of the checklist approach to testing—the data will be produced because they are 'missing', not because they are needed for any justifiable scientific purpose. Secondly, there are proposals for introducing animal tests for endocrine disruption potential, again without the strong justification of scientific necessity, without proper valida-

tion, and based on erroneous toxicological principles such as the belief that the application of high, acutely toxic doses can be used to predict the effects of repeated, low doses. Thirdly, there is the risk that nationalism and the 'not invented here' syndrome will slow down, or even prevent, the acceptance of procedures which involve fewer animals, will cause less suffering, or can replace animal use altogether, merely because they were not developed in a particular country. A similar attitude may prevent the removal from the approved lists of test guidelines of inhumane animal procedures which can be replaced in line with the Three Rs, such as the classical LD50 test.

My hope, of course, is that these kinds of problems can be avoided, and I see genuine commitment to sound and sensible progress based on the 58 recommendations of *The Three Rs: the Way Forward*, the report and recommendations of a workshop organized by ECVAM and CAAT (Balls *et al.* 1995), which was attended by William Russell and Rex Burch, as the means whereby this could best be achieved.

I will close with two further quotations from *The Principles of Humane Experimental Technique*, which provide an appropriate foundation for what will be accomplished as a result of this *International Conference on the Use of Humane End-points in Animal Experiments for Biomedical Research*, especially if you will accept a suggestion that the Conference is really about the need for *less-inhumane* (or *more-humane*) procedures, given that many of the procedures currently in use inevitably cause considerable pain, suffering, distress or lasting harm.

Firstly, on *science and humanity*, Russell and Burch said that the seemingly irreconcilable conflict between the claims of science and medicine and those of humanity 'disappear altogether on closer inspection; it is now widely recognized that the humanest possible treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiments'.

Secondly, in spelling out what I like to call the *humanity criterion*, they said: 'If we are to use a criterion for choosing experiments to

perform, the criterion of humanity is the best we could possibly invent. The greatest scientific experiments have always been the most humane and the most aesthetically attractive, conveying that sense of beauty and elegance which is the essence of science at its most successful'.

References

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